REMARKS

Upon entry of the foregoing amendment, claims 1-13, 17-20, and 32-34 are pending in this application. Claims 17-20 are withdrawn from consideration as being directed to a non-elected invention. Claims 14-16 and 21-31 have been previously cancelled without prejudice or disclaimer of the canceled subject matter. Applicants maintain the right to file one or more continuation or divisional applications on any canceled subject matter. Claims 5, 9, 10, 32, 33, and 34 are amended herein. Amendments to the claims are made without prejudice to, or disclaimer of, the canceled subject matter.

Claim 5 is amended to more clearly identify that the fragment is a nucleic acid fragment comprising at least 12 consecutive nucleotides. Support for the amendment to the claim is found, for example, on page 13, line 1, and elsewhere throughout the specification.

Claims 9 and 10, as newly amended here, now recite "ten" contiguous nucleotides. Support for the amendment to the claim is found, for example, on page 12, lines 1-4 (reciting "at least about 8"); and, elsewhere throughout the specification. Claims 9 and 10 were also amended to correct grammatical errors.

Claim 32 is amended to now recite the nucleotide sequence has at least 10 nucleotides. Support for the amendment to the claim is found, for example, on page 12, lines 1-4 (reciting "at least about 8"); and, elsewhere throughout the specification. Claim 32 is also amended ("hybridizes") to more clearly claim the invention. Support for the amendment to the claim is found, for example, in original claim 32, and, elsewhere throughout the specification.

Claims 33 and 34 have been amended to more clearly claim the invention as suggested by the Examiner. Support for the amendments to the claims is found, for example, within original claims 33 and 34, and, elsewhere throughout the specification.

Additionally, Applicants maintain the right to pursue the subject matter of SEQ ID NO: 1450 and its counterpart polypeptide in a divisional application.

1. Restriction Requirement

Applicants acknowledge the finality of the restriction requirement.

2. Information Disclosure Statement

Applicants acknowledge with thanks the return of executed PTO 1449 forms by the Examiner.

3. Sequence Rule Non-Compliance

The Office asserts this application allegedly fails to comply with the requirement of 37 C.F.R. §§ 1.821-1.825 in that the specification discloses nucleic acid sequences on page 79 not identified by sequence identifier numbers (SEQ ID NOs). In reply, submitted herewith is an updated sequence listing, a Statement, and an updated computer readable form (CRF). Also, the specification has been amended to include SEQ ID NOs. 7545 and 7546 where necessary.

4. Priority Information

In reply to the Examiner's instructions to update the priority data, the priority information set forth on page 1 of the application was previously updated in the preliminary amendment filed December 1, 2003 and has been updated again herein to include the patent number of application no. 09/134,001, filed August 13, 1998. The priority information in the application is currently believed to be correct.

5. Specification Informalities and Objections

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure without complete evidence that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of biological materials. The objection is traversed as discussed in Section 6.

6. Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1-13 and 32 stand rejected under 35 U.S.C., § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The rejection is respectfully traversed.

At page 5 of the Office Action, the Office has required a copy of the deposit statement in order to meet the requirements of 35 U.S.C. § 112, first paragraph. The Office alleges that "since there are several applications, each with a different SEQ ID NO. from a genomic sequence of *S. epidermis* has been filed in the Office and these applications have been assigned to various examiners in [the] 1600 technology center. It is not clear whether the claimed sequences are part of the ATCC deposit or something else."

Contrary to the position of the Office, a deposit is not required, if the nucleotide or amino acid sequences having the claimed (or disclosed) sequence identifiers are presented in the specification. The sequence listing of the claimed nucleotide and amino acid sequences for this application are freely available both to the public and to the Examiner via the PTO website (*see*, "Publication Site for Issued and Published Sequences" (PSIPS)). Submitted herewith is the printout of the claimed amino acid sequence of SEQ ID NO. 6352 (Exhibit A) and the nucleotide sequence of SEQ ID NO. 2580 (Exhibit B). Translation of nucleotide sequence SEQ ID NO: 2580 via publicly available software ("WWW Nucleotide Translation") gives the amino acid sequence of SEQ ID NO: 6352. A copy of the translation (in all 6 frames) is attached (Exhibit C). It is noted that the translated sequence has 335 amino acids, not 336 (as is printed at the top of the print out). In addition, a deposit statement is not required, because it is the sequences which are claimed, not the deposited organism.

The rejection is believed to be overcome. Reconsideration and withdrawal of the rejection is respectfully requested.

7. Rejections Under 35 U.S.C. § 112, First Paragraph

At page 6 of the Office Action, claims 1-13 and 32 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. The rejection is respectfully traversed.

The Office alleges the fragments/variants or immunogenic compositions for the treatment or prevention of *S. epidermidis* infection do not meet the guidelines on written description. The Office further states that "[r]ecitation of 'isolated DNA sequences encoding a polypeptide comprising SEQ ID NO. 6352' in the claims is interpreted as isolated DNA encoding a polypeptide which comprises a part of SEQ ID NO + unlimited/unknown

sequence (emphasis added)." However, that interpretation is incorrect. The "comprising" refers to the isolated nucleic acid of "[a]n isolated nucleic acid" and **not to the nucleotide sequence encoding the *S. epidermidis* polypeptide of SEQ ID NO: 6352**. The Office then continues "similarly, recitation of 'a polypeptide' or 'a nucleic acid' in the claims is viewed as something less than the polypeptide or less than the nucleic acid sequence." This interpretation is also incorrect. A "polypeptide" is not the same as, for example "a fragment of a polypeptide" or "a polypeptide, or fragment thereof."

Based on the incorrect claim interpretation of the term "comprising," the Office then rejects the claims on the basis that the specification does not disclose an isolated DNA sequence encoding a polypeptide comprising SEQ ID NO: 2580 + unlimited/unknown sequences. Contrary to the position of the Office, a claim reciting the term "comprising" has open claim language and such claims are permissible under U.S. patent law. *See*, for example, M.P.E.P. § 2111.03, "Transitional Phrases," page 2100-53, right column, top paragraph, Rev. 3, August 2005, citing *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501, 42 U.S.P.Q.2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim."). Thus, the isolated nucleic acid of claim 1, for example, comprises a nucleotide sequence encoding an *S. epidermidis* polypeptide of SEQ ID NO: 6352, as well as additional elements which are not, and are not required to be, specified. Other elements may be added, as disclosed in the specification, such as for example, promoter sequences; sequences encoding second polypeptide portions for generation of fusion proteins (*see*, for example, pages 10, lines 12-21); and, transcriptional regulatory sequences (*see*, for example, page 11, lines 24-27). These sequences are well known in the art but are not essential to the claim.

The Office argues that the specification fails to satisfy the written description requirement, because the specification allegedly fails to teach the identifying characteristics of the fragments/variants of nucleic acid or immunogenic compositions for the treatment or prevention of *S. epidermidis* infection. However, contrary to the position of the Office, the specification discloses methods for identifying characteristics of the fragments/variants. *See*, for example, page 62, beginning at line 18, disclosing that critical residues of a polypeptide involved in molecular recognition of the polypeptide can be determined and used to generate

S. epidermidis derived peptidomimetics that would competitively or noncompetitively inhibit binding of the polypeptide with the interacting polypeptide. *See also*, for example, page 64, describing screening assays to identify *S. epidermidis* peptides which stimulate T cells.

The Office argues that the written description requirement is not satisfied because the specification allegedly fails to disclose the claimed fragments/variants. However, contrary to the position of the Office, once the amino acid sequence and the nucleotide sequence are known, the variants and fragments thereof are also known particularly when the claimed segments are contiguous or consecutive. Reconsideration and withdrawal of the rejection is respectfully requested.

8. Rejections Under 35 U.S.C. § 112, First Paragraph

At page 9 (¶10) of the Office Action, claims 1-13 and 32 are rejected under 35 U.S.C. §112, first paragraph. The Office argues that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The rejection is respectfully traversed.

The Office arguments spanning pages 9-15 are believed to be summarized below and fully addressed by the arguments that follow. The Office argues that:

> 1) allegedly the specification does not reasonably provide enablement for an isolated nucleic acid or immunogenic composition for the treatment or prevention of *S. epidermidis* comprising the compositions of claims 1, 5, 10 and 32. Office Action, at page 9, line 11 through page 10, line 4;
>
> 2) allegedly the specification fails to provide an enabling disclosure for the full scope of the claimed nucleic acids, because it fails to provide any guidance regarding how to make and use the isolated nucleic acid or isolated nucleic acid encoding a polypeptide. Specifically, the Office asserts the specification allegedly fails to disclose how a nucleotide sequence of at least 8 nucleotides plus other nucleic acid sequences would hybridize under high stringency conditions to SEQ ID NO: 2580 since the

> specification provides no disclosure of fragments or variants with a specific function. Office Action, at page 10, line 6 through page 12, line 7; and,

Contrary to the arguments of the Office, the specification (*see*, for example, page 21, lines 9-20) discloses a method using high and low stringency hybridization conditions. Methods of hybridization are well known in the art. *See*, for example, specification page 26, line 18 through page 27, line 14, which refers to a large number of books and other references for their teachings which are well known in the art at the time. The Office is reminded that Applicants are not required to teach that which is well known to one of ordinary skill in the art. In addition, the function of the various fragments or variants can easily be determined by one of skill in the art. The instant invention provides libraries of nucleic acids, which provide probes, primers, and markers used in epidemiological studies (*see*, for example, page 30, lines 8-10). The library of nucleic acids also provides sequences comprising or encoding targets for therapeutic drugs (*see*, for example, page 30, lines 10-11).

> 3) allegedly the specification fails to teach the critical protein residues involved in the function of the protein encoded by SEQ ID NO: 2580, such that the artisan allegedly would not have been provided with guidance to test, screen or make the nucleic acid sequence variants of SEQ ID NO: 2580 or encoding variants of polypeptide 6352. The Office argues that single amino acid or nucleotide changes can destroy the function of a biomolecule; that there is an unpredictable relationship between sequence and function; that protein chemistry is a very unpredictable area of biotechnology (relying on four journal articles covering a wide variety of proteins for support); that the specification fails to provide the function of the full-length protein; that it is unclear exactly what the composition of any protein will be if it is expressed by a nucleic acid which has the claimed fragments; and, that the specification has not shown that modifying a reference

> sequence encoding a reference polypeptide will automatically predict the production of a polypeptide for use in any assay. Office Action, at page 11, line 3 through page 14, line 16.

Contrary to the arguments of the Office, the specification provides the definition of "fragment" (*see*, for example, page 24, lines 7-14) and states that fragments can be generated by methods known in the art. Further, changes in function of proteins having sequences altered by deletion, insertion, or alteration of amino acids are readily determined by one of skill in the art using methods readily known and widely available (*see*, for example, page 37, line 1 through page 39, line 5, describing methods by the function of a gene can be ascertained). Changes or alterations that result in non-functional proteins could have been easily determined by one of ordinary skill using methods available in the art at the time. No prediction of a polypeptide is claimed in the claims herein. The Office is reminded that Applicants are not required to teach that which is well known to one of ordinary skill in the art.

In view of the teachings of the specification and the recognized teachings in the art, the rejection of claims 1-13 and 32 is believed to be overcome. It is noted that claims 1-4 are improperly rejected under this section, because claim 1 does not suffer from the alleged deficiencies. Reconsideration and withdrawal of the rejection is respectfully considered.

9. Rejections Under 35 U.S.C. § 112, Second Paragraph

At page 16 of the Office Action, the Office rejects claims 33 and 34 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. The rejection is respectfully traversed.

The Office alleges that the claim language of claims 33 and 34 is vague, because (for example) "isolated nucleic acid does not contain SEQ ID NO: 2580." In reply, and without acquiescing to the correctness of the rejection, claims 33 and 34 have been amended to comply in part with the claim language suggested by the Office. It is noted the term "nucleic acid" or "polynucleotide" is the plural of "nucleotides" and the term "polynucleic acid" is believed to be redundant.

In view of the amendments to the claims, the rejection is believed to be overcome. Reconsideration and withdrawal of the rejection is respectfully requested.

10. Claim Rejections Under 35 U.S.C. § 102(b)

At page 16 of the Office Action, claims 1, 5, 9, 10, and 32 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Goh *et al.*, 1996 *Clin. Microbiol.* 34(4): 818-23 ["Goh"]. The rejection is respectfully traversed.

Goh generates probes using nucleotide sequences from *S. epidermidis* 9759 ["SE 9759"], not *S. epidermidis* 18972 ["SE18972"] as claimed in the instant specification.

The Office asserts that in the absence of evidence to the contrary, the disclosed prior art PCR product (nucleic acid) would allegedly inherently contain the claimed nucleic acid "as the use of PCR coupled with restriction endonuclease analysis of PCR product has proven to be sensitive and specific in the art." The Office further argues the burden is on Applicants to show a novel or unobvious difference between the claimed product and the product of the prior art.

At the outset, Applicants note that Goh' *S. epidermidis* strain (SE 9759) is a different strain than Applicants' *S. epidermidis* strain SE18972. Contrary to the arguments of the Office, Goh does not "inherently" teach the amino acid sequence of SEQ ID NO: 6352 (or, the nucleotide sequence SEQ ID NO: 2580). Goh discloses, *inter alia,* production of primers to heat shock protein 60 ("HSP60") (*see*, Abstract). Applicants' protein comprises SEQ ID NO: 6352 and is not a HSP, let alone HSP60.

Although the amino acid sequence of the HSP60 disclosed by Goh is publicly available (*see*, Exhibit D, showing the results of the NCBI data base search for the Goh HSP60 sequence), the nucleotide sequence of the genome of Goh's *S. epidermidis* strain 9759 is not publicly available (*see*, Exhibit E, listing the bacterial genomes publicly available in the NCBI genome data base). In addition, a search of the scientific literature also failed to uncover any references showing that any other sequences from Goh's 9759 strain have been published. *See*, Exhibit F, search results of PubMed (PM) and PubMed Central (PMC) (both PM and PMC are literature data bases available through NCBI), showing no other citations related to *S. epidermidis* strain 9759. Although two *S. epidermidis* genomic sequences are publicly available, *S. epidermidis* ATCC12228 and *S. epidermidis* RP62A, **neither genomic**

sequence is available as prior art, because the dates of submission to the NCI database, or publication, are subsequent to the priority date of this application (claiming priority at least to Nov. 29, 1999). The genomic nucleotide sequence of *S. epidermidis* RP62A was completed 01/09/2002 and published in April 2005 (Gill *et al.*, J. Bacteriol. 2005 Apr; 187(7):2426-38)["Gill"] (*see*, Exhibit G, page 1, showing the sequence completion date, and page 3, showing publication date of Gill). The genomic nucleotide sequence of *S. epidermidis* ATCC 12228 was completed 01/02 2003 and published in September 2003 (Zhang *et al.*, Mol. Microbiol. 2003 Sep; 49(6): 1577-93["Zhang"]) (*see*, Exhibit H, page 1, showing the sequence completion date and page 3 showing publication date of Zhang).

As the Office is aware, the Examiner must provide rationale or evidence tending to show inherency ("In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Inter. 1990)). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 U.S.P.Q.2d 1949, 1950-51 (Fed. Cir. 1999). Mere allegations of inherency based on "use of PCR coupled with restriction endonuclease analysis" and that such techniques have "proven to be sensitive and specific in the art" are irrelevant in establishing inherency, because the genomic nucleic acid sequence is not available. Because the Office has failed to provide evidence showing the protein having SEQ ID NO: 6352 is "necessarily present" in Goh's 9759 *S. epidermidis* strain, the Office has failed to establish inherency.

Goh does not anticipate claims 1, 5, 9, 10, and 32, because there is no evidence showing the Goh teaches, or inherently discloses, the protein having SEQ ID NO: 6352 (or

the nucleotide sequence SEQ ID NO: 2580). Reconsideration and withdrawal of the rejection is respectfully requested.

11. Claim Rejections Under 35 U.S.C. § 102(e)

At page 18 of the Office Action, the Office rejects claims 1, 5, 9, 10, and 32 under 35 U.S.C. § 102(e) as being unpatentable over U.S.P.N. 5,770,375 (Ohno *et al.*) ["Ohno"]. The rejection is respectfully traversed.

The Office states (page 18, last line to page 19, line 2) that "[s]imilarly the disclosed nucleic acid reads on the fragments as in claim 5 and a nucleotide sequence (less than full length or more than one nucleic acid) as in claim 1." However, the Office has incorrectly interpreted the claim language of claim 1.

The word "comprising" refers to the isolated nucleic acid and **not** to the nucleotide sequence encoding the *S. epidermidis* polypeptide. Claim 1 recites "[a]n isolated nucleic acid comprising a nucleotide sequence encoding an *S. epidermidis* polypeptide of SEQ ID NO: 6352." At the very least, any applicable prior art must teach "a nucleotide sequence encoding an *S. epidermidis* polypeptide of SEQ ID NO: 6352." While the claimed isolated nucleic acid may comprise other nucleotides, or nucleic acid sequences in addition to the "nucleotide sequence encoding an *S. epidermidis* polypeptide of SEQ ID NO: 6352," it must contain at least "the nucleotide sequence encoding an *S. epidermidis* polypeptide of SEQ ID NO: 6352." Contrary to the Office, any prior art document teaching a partial sequence ("less than full length"), or "more than one nucleotide" of an *S. epidermidis* nucleic acid sequence, does not teach, or suggest, the isolated nucleic acid claimed in claim 1.

In addition, Applicants have performed a BLAST analysis (using the BLAST program available through the NCBI database) of SEQ ID NO: 2580 (the nucleotide sequence encoding the *S. epidermidis* polypeptide having SEQ ID NO: 6352) against Ohno SEQ ID NOs: 5, 6, 7, and 8 and have found there is no significant similarity between the *S. epidermidis* nucleotide sequences of Ohno and the claimed nucleotide sequence (SEQ ID NO: 2580) of *S. epidermidis* 18972. Applicants have also performed a comparison of SEQ ID NO: 6352 (the amino acid sequence) with the translated sequences encoded by SEQ ID NOs; 5, 6, 7 and 8 of Ohno and have not found any significant similarity. Thus, the rejection

of claim 1 as being anticipated by Ohno is in error. Claim 1, and dependent claims 2-4, are therefore free of the art.

Regarding claim 5, claim 5 has been amended to recite a polypeptide fragment comprising at least 4 consecutive amino acids (12 nucleotides) and thus is believed to overcome the rejection over Ohno (having a 9 consecutive nucleotide sequence). Since claim 5 is now free of the art, dependent claims 6-8, 11-13 are also patentable over Ohno.

Claim 9 has been amended to recite a nucleotide sequence of at least 10 consecutive nucleotides, and is thus patentable over Ohno (reciting a sequence of 9 nucleotides). Claim 10 has been amended to recite a sequence of at least 10 nucleotides in length, and is now patentable over Ohno. Claim 32 has been amended to recite that the nucleotide sequence comprises at least 10 nucleotides. Claim 32 is now patentable over Ohno.

In view of the arguments above and amendments to the claims, claims 1, 5, 9, 10, and 32 are believed to be patentable over Ohno. Reconsideration and withdrawal of the rejection is respectfully requested.

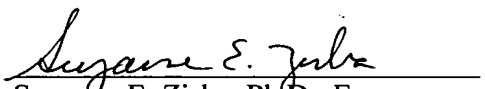
CONCLUSION

In conclusion, this amendment and reply is believed to be a full response to the outstanding Office Action. Should any issues remain outstanding or if there are any questions concerning this paper, or the application in general, the Examiner is invited to telephone the undersigned representative at the Examiner's earliest convenience.

EXCEPT for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No. 50-0573. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

Date: March 21, 2006

Respectfully submitted,



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